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under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

***Amendments***

***In the Claims:***

Please cancel claims 1-27 without prejudice or disclaimer.

Please add the following claims 28-83:

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28. (New) A method for identifying a compound that inhibits the ubiquitination reaction mediated by the Anaphase Promoting Complex (APC), comprising

(a) reacting APC11, ubiquitin, and a test compound under conditions and duration of time sufficient to obtain a measurable level of multiubiquitin chains in the absence of said test compound; and

(b) determining said test compound's ability to interfere with the formation of multiubiquitin chains by APC11;

wherein said reaction is made in the absence of APC subunits other than APC11.

29. (New) The method of claim 28, wherein said reaction step (a) further includes a ubiquitin activating enzyme (E1), a ubiquitin conjugating enzyme (E2), and ATP, and the level of multiubiquitin chains formed in the presence of said test compound

is compared to the level of multiubiquitin chains formed in the absence of said test compound.

30. (New) The method of claim 29, wherein said APC11 is human.

31. (New) The method of claim 29, wherein said E1 is wheat UBA1.

32. (New) The method of claim 29, wherein said E2 is the human variant UBCH5b.

33. (New) The method of claim 29, wherein the formation of multiubiquitin chains is measured using an antibody.

34. (New) The method of claim 33, wherein said antibody is specific for APC11.

35. (New) The method of claim 33, wherein said antibody is specific for ubiquitin.

36. (New) The method of claim 33, wherein said antibody is labeled for detection.

37. (New) The method of claim 36, wherein said antibody is labeled with a fluorimetric label, a radioactive label, or an enzymatic label.

38. (New) The method of claim 29, wherein said formation of multiubiquitin chains is measured using fluorescence resonance energy transfer (FRET).

39. (New) The method of claim 29, wherein one or more assay component selected from the group consisting of APC11, E1, E2 and ubiquitin is fused to an affinity tag.

40. (New) The method of claim 39, wherein said affinity tag is glutathione S-transferase, maltose binding protein, His(6), myc-epitope, biotin, or HA-epitope.

41. (New) The method of claim 39, wherein said assay component fused to said affinity tag is APC11.

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42. (New) The method of claim 39, wherein said assay component fused to said affinity tag is E2.

43. (New) The method of claim 39, wherein said assay component fused to said affinity tag is ubiquitin.

44. (New) The method of claim 39, wherein more than one assay component is fused to said affinity tag.

45. (New) The method of claim 39, wherein said assay component is detected with an antibody specific for said affinity tag.

46. (New) A method for identifying a compound that inhibits the ubiquitination reaction mediated by the Anaphase Promoting Complex (APC), comprising

(a) reacting APC11, ubiquitin, an APC substrate, and a test compound under conditions and duration of time sufficient to obtain a measurable level of multiubiquitin chains on said substrate in the absence of said test compound; and

(b) determining said test compound's ability to interfere with the formation of multiubiquitin chains on said substrate by APC11;

wherein said reaction is made in the absence of APC subunits other than APC11.

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47. (New) The method of claim 46, wherein said reaction step (a) further includes a ubiquitin activating enzyme (E1), a ubiquitin conjugating enzyme (E2), and ATP, and the level of multiubiquitin chains formed in the presence of said test compound is compared to the level of multiubiquitin chains formed in the absence of said test compound.

48. (New) The method of claim 47, wherein said APC11 is human.

49. (New) The method of claim 47, wherein said APC substrate is CyclinB.

50. (New) The method of claim 47, wherein said APC substrate is Securin.

51. (New) The method of claim 47, wherein said E1 is wheat UBA1.

52. (New) The method of claim 47, wherein said E2 is the human variant UBCH5b.

53. (New) The method of claim 47, wherein the formation of multiubiquitin chains is measured using an antibody.

54. (New) The method of claim 53, wherein said antibody is specific for APC11.

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55. (New) The method of claim 53, wherein said antibody is specific for ubiquitin.

56. (New) The method of claim 53, wherein said antibody is labeled for detection.

57. (New) The method of claim 56, wherein said antibody is labeled with a fluorimetric label, a radioactive label, or an enzymatic label.

58. (New) The method of claim 47, wherein said formation of multiubiquitin chains is measured using fluorescence resonance energy transfer (FRET).

59. (New) The method of claim 47, wherein one or more assay component selected from the group consisting of APC11, E1, E2 and ubiquitin is fused to an affinity tag.

60. (New) The method of claim 59, wherein said affinity tag is glutathione S-transferase, maltose binding protein, His(6), myc-epitope, biotin, or HA-epitope.

61. (New) The method of claim 59, wherein said assay component fused to said affinity tag is APC11.

A1 62. (New) The method of claim 59, wherein said assay component fused to said affinity tag is E2.

63. (New) The method of claim 59, wherein said assay component fused to said affinity tag is ubiquitin.

64. (New) The method of claim 59, wherein more than one assay component is fused to said affinity tag.

65. (New) The method of claim 59, wherein said assay component is detected with an antibody specific for said affinity tag.

66. A method for identifying a compound that inhibits the self-ubiquitination reaction mediated by the Anaphase Promoting Complex (APC), comprising

(a) reacting APC11, ubiquitin, and a test compound under conditions and duration of time sufficient to obtain a measurable level of ubiquitination of APC11 in the absence of said test compound; and

(b) determining said test compound's ability to interfere with the ubiquitination of APC11.

AI 67. (New) The method of claim 66, wherein said reaction step (a) further includes a ubiquitin activating enzyme (E1), a ubiquitin conjugating enzyme (E2), and ATP, and the level of ubiquitination of APC11 in the presence of said test compound is compared to the level of ubiquitination of APC11 in the absence of said test compound.

68. (New) The method of claim 67, wherein said APC11 is human.

69. (New) The method of claim 67, wherein said E1 is wheat UBA1.

70. (New) The method of claim 67, wherein said E2 is the human variant UBCH5b.

71. (New) The method of claim 67, wherein said ubiquitination of APC11 is measured using an antibody.



72. (New) The method of claim 71, wherein said antibody is specific for APC11.

73. (New) The method of claim 71, wherein said antibody is specific for ubiquitin.

74. (New) The method of claim 71, wherein said antibody is labeled for detection.

75. (New) The method of claim 74, wherein said antibody is labeled with a fluorimetric label, a radioactive label, or an enzymatic label.

76. (New) The method of claim 67, wherein said formation of multiubiquitin chains is measured using fluorescence resonance energy transfer (FRET).

77. (New) The method of claim 67, wherein one or more assay component selected from the group consisting of APC11, E1, E2 and ubiquitin is fused to an affinity tag.

78. (New) The method of claim 77, wherein said affinity tag is glutathione S-transferase, maltose binding protein, His(6), myc-epitope, biotin, or HA-epitope.

79. (New) The method of claim 77, wherein said assay component fused to said affinity tag is APC11.

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80. (New) The method of claim 77, wherein said assay component fused to said affinity tag is E2.

81. (New) The method of claim 77, wherein said assay component fused to said affinity tag is ubiquitin.

82. (New) The method of claim 77, wherein more than one assay component is fused to said affinity tag.

83. (New) The method of claim 77, wherein said assay component is detected with an antibody specific for said affinity tag.

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